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POLYBROMODIBENZO-P-DIOXINS AND FURANS THEIR MIXED BROMO/CHLORO ANALOGUES: A REVIEW OF THE LITERATURE ON SOURCES, METHODS OF ANALYSIS, ENVIRONMENTAL DISTRIBUTION AND TOXICITIES

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1.0 INTRODUCTION

As a result of their wide distribution and persistence in the environment, and the high toxicities exhibited by certain congeners, much information has accumulated over the past two decades on the synthesis, analysis, environmental distribution and biological activity of polychlorinated dibenzo-p-dioxins (PCDDs) and furans (PCDFs). PCDDs and PCDFs have been found as trace contaminants in certain commercial chemical products prepared from chlorinated aromatic compounds, particularly chlorinated phenols and their phenoxyacetic acid derivatives, and polychlorinated biphenyls. In addition to these chemical sources, PCDDs and PCDFs are also often generated during combustion or other high-temperature processes whenever organic matter and a suitable source of chlorine are present.

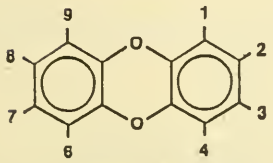
More recently, there has been increasing concern regarding the potential environmental impact of polybrominated dibenzo-p-dioxins (PBDDs), furans (PBDFs) and mixed bromochloro dibenzo-p-dioxins (BCDDs) and furans (BCDFs). These compounds are of particular interest owing to their structural similarities to the PCDDs and PCDFs. As with the chlorinated analogues, PBDDs and PBDFs have been found as impurities in commercial products and both PBDD/Fs and BCDD/Fs have been observed as thermal reaction products from appropriate precursors. In addition, these compounds are expected to exhibit biological activities similar to those of their chlorinated analogues and, hence their presence in the environment is a cause for concern.

STRUCTURAL CONSIDERATIONS; ISOMER AND CONGENER NUMBERS
(Buser, 1987a)

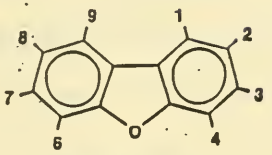
The molecular structures of the parent compounds, dibenzo-p-dioxin (DD) and dibenzofuran (DF), and the numbering systems used in making derivatives, are shown in Table 1. As summarized in the table, with bromine and/or chlorine substitution, a total of 5020 halogenated derivatives (1700 dioxins and 3320 furans) is possible. These may be divided, according to halogen content, into 44 congener groups having partial general formula Br_xCl_y, where x,y = 0,1...8 and x + y = 1,2...8. The numbers of isomers in each congener group are also summarized in the table.

TABLE 1

Structures, Numbering Systems, and Isomer/Congener Numbers for Halogenated (Bromo, Chloro) Dibenzo-p-dioxins and Dibenzofurans



Dibenzo-para-dioxin



Dibenzofuran

Numbers of possible halogennted (Br_xCl_y) isomers

		Br_x										Br_x								
		0	1	2	3	4	5	6	7	8		0	1	2	3	4	5	6	7	8
	0	-	2	10	14	22	14	10	2	1		-	4	16	28	38	28	16	4	1
	1	2	14	42	70	70	42	14	2			4	28	28	140	140	84	28	4	
	2	10	42	114	140	114	42	10				16	84	216	280	216	84	16		
	3	14	70	140	140	70	14					28	140	280	280	140	28			
Cl_y	4	22	70	114	70	22						38	140	216	140	38				
	5	14	42	42	14							28	84	84	28					
	6	10	14	10								16	28	16						
	7	2	2									4	4							
	8	1										1								
Total 1700 (75 PCDDs, 75 PBDDs, 1550 BCDDs)												Total 3320 (135 PCDFs, 135 PBDFs, 3050 BCDFs)								

Congener groups and number of isomers within the groups

Substitution	No. of Congener Groups	No. of DDs	No. of DFs
mono	2	4	8
di	3	34	60
tri	4	112	224
tetra	5	298	572
penta	6	448	896
hexa	7	472	912
hepta	8	256	512
octa	9	76	76
Total	44	1700	3320

2.0 SOURCES

The PBDD/Fs and the BCDD/Fs are not made intentionally, except where they are needed in small quantities for research and/or chemical analysis.

As with their chloro analogues, they have been found as either contaminants in commercial chemicals or as products of thermal processes (ie. heating, pyrolysis, combustion, incineration).

As of the writing of this report, the major, known sources of these compounds are as summarized below.

2.1 CONTAMINANTS IN COMMERCIAL BROMINATED AROMATIC CHEMICALS

The USEPA has promulgated a testing and reporting rule, under the Toxic Substances Control Act (TSCA), for chemicals that may be contaminated with chlorinated and brominated DDs and DFs. A list of the chemicals subject to testing and/or reporting, and a summary of the status of the testing and reporting, have been published (Remmers, 1991).

The major use of the brominated aromatic derivatives is as flame retardants in a wide range of consumer products, including carpets, mattresses, plastics, paints, paper, wood, adhesives, electrical cables, protective coatings and clothing. Materials treated with flame retardant chemicals are able to resist burning when exposed to relatively low energy ignition sources such as cigarettes, matches, candles and stove burners. The potential environmental impact

of flame retardants, of possible toxic contaminants in them and of products of thermal reaction has been of concern for some time (Hutzinger, 1976 and 1987).

Structures of the principal organic compound types used as flame retardants are summarized in Table 2. It has been estimated that the rate of consumption of brominated flame retardants in the U.S. is at least 36 million pounds per annum (Donnelly, 1990).

A flame retardant may be classified as reactive or additive depending on how it is incorporated into the treated polymeric material. Reactive flame retardants (eg. tetrabromophthalic anhydride) are chemically bonded to the polymeric matrix either by grafting or by copolymerisation. Additive flame retardants (eg. polybromodiphenyl ethers) are simply blended physically with the polymer and may gradually escape from the treated material (eg. upon laundering; Gutenmann, 1975).

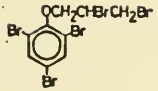
While one or more of the six elements bromine, chlorine, phosphorous, nitrogen, boron and antimony, are commonly used in flame retardant formulations (Blum, 1977), bromine is believed to be the most effective (Hutzinger, 1976). Indeed, bromine-containing flame retardants exhibit the greatest structural diversity (Liepins, 1976). They are thought to suppress combustion by acting as free radical traps, therby removing those chemical species which are required to maintain combustion (Blum, 1977; Sanders, 1978). Treated thermoplastics typically contain 5-20%, by weight, of brominated flame retardants and antimony trioxide (Sb_2O_3) is frequently incorporated as a co-retardant.

TABLE 2

Structures of Some Brominated Organic Flame Retardants
(Hutzinger, 1976)

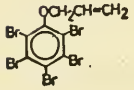
Polybromobenzenes

Polybromophenols

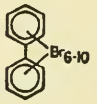


2,4,6-Tribromophenoxy-2,3-dibromo-propane

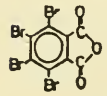
Pentabromotoluene



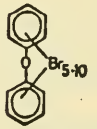
1-(Pentabromophenoxy)-propene(2)



Polybromobiphenyls

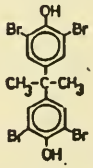


Tetrabromophthalic anhydride

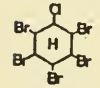


Polybromodiphenyl ethers

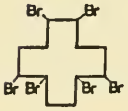
2,5-Dibromoterephthalic acid



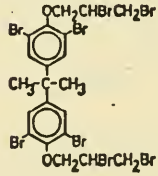
Tetrabromobisphenol A



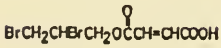
Pentabromochlorocyclo-hexane



Hexabromocyclododecane



2,2-Bis-[4-(2,3 dibromopropoxy)-3,5 dibromopheny]-propane



Mono-2,3-dibromopropyl maleate

There are relatively few reports of the analysis of flame retardant chemicals, or of material treated with them, for PBDDs or PBDFs, probably because of the difficulties associated with obtaining reliable results (see section 3.0). Both PBDDs and PBDFs (ppb level) were found in a technical grade sample of 2,4,6-tribromophenol, but not in analytical grade pentabromophenol or tetrabromophthalic anhydride (Thoma, 1986b). PBDFs (ppb level), but no PBDDs, were found in tetrabromobisphenol A (TBBA) (Thoma, 1986b; Thies, 1990), and in much higher concentrations (ppm level) in polybromodiphenyl ether (PBDPE) samples (Donnelly, 1989a; Hileman, 1989). In studies of thermoplastic resins containing PBDPE flame retardants (high-impact polystyrene: HIPS/Br_{10}DPE, polybutylene terephthalate: PBT/Br_{10}DPE, acrylonitrile-butadiene-styrene: ABS/Br_8DPE), PBDFs, but no PBDDs, were found (Donnelly, 1989a; McAllister, 1990). The former authors report that the levels of PBDFs increase when the resins are processed, particularly when they are extruded under extreme conditions of time and temperature. They report (McAllister, 1990) increases in PBDF levels only under abusive treatment conditions. No significant changes were found in the levels of PBDFs or PBDDs in several TBBA-containing polymers after heating at 240°C (Thies, 1990), a typical processing temperature.

2.2 THERMAL TREATMENT OF FLAME RETARDANTS AND PRODUCTS CONTAINING THEM

It is well-known that PCDDs and PCDFs can be formed from chlorinated aromatic derivatives as a result of thermally induced reactions. For example, the conversion into PCDDs and PCDFs has been demonstrated for chlorophenols, polychlorinated biphenyls, polychlorinated diphenyl ethers and chlorobenzenes (ref. 5-9 in Buser, 1986b). Concern that

the brominated analogues would likely undergo similar conversions into potentially toxic PBDDs and PBDFs has generated considerable interest in the products of pyrolysis and/or combustion of brominated flame retardants. Such products are expected to be released into the environment as a result of accidental fires or of disposal of fire retardant-containing materials by incineration. Indeed, there is a report of evidence for PBDFs and lesser amounts of PBDDs and mixed bromochloro analogues in soot from a fire in a bowling alley (Buser, 1986a).

Virtually all of the information available on the formation of PBDDs and PBDFs upon pyrolysis of brominated flame retardants comes from laboratory-scale experiments. Table 3 summarizes the substrates investigated and the thermal conditions employed (apparatus, temperatures, times) for studies reported in the literature. While some experiments have involved simply heating samples in open or sealed vials or tubes, most pyrolysis experiments have been carried out in appartus designed to mimic a range of conditions which might be encountered in waste incinerators or in fires.

The first report of the formation of PBDDs or PBDFs upon pyrolysis of a brominated flame retardant seems to have been that made by O'Keefe in 1978 (O'Keefe, 1978). In this study, pyrolysis of Firemaster FF-1 (major component 2,2',4,4',5,5'-hexabromobiphenyl) in an open tube (380-400°C) gave products identified by gas chromatography/mass spectrometry (GC/MS) as Br_4DF (40 ppm) and Br_5DF (4 ppm). The GC retention time and MS fragmentation pattern of the tetrabromodibenzofuran corresponded to those of 2,3,7,8-

TABLE 3

Thermolyses of Brominatedd Flame Retardants and of Polymers Containing Them		
Publication	Substrates Investigated [a]	Mode of Thermal Treatment
Alsabbagh	2,4,6-tribromoaniline; N-tribromophenylmaleimide	Sealed tube; 550-640°C; 1-2 min.
Buser, 1986b	Commercial PBDPEs (penta-, octa- and deca-bromo)	Open vials; 510-630°C; 60 sec.
Donnelly, 1989b	PBT resin with PBDPE fire retardant	In air stream; 400°C; 10 min.
Dumler, 1989a	PBT/Br_{10}DPE/Sb_2O_3	DIN, BIS, VCI[c]; 300-800°C at 100° intervals
Dumler, 1989b	Polystyrene/Br_{10}DPE/Sb_2O_3; polypropylene/Br_{10}DPE/Sb_2O_3; ABS/Br_8DPE/Sb_2O_3; polyurethane/Br_5DPE; ABS/1,2-bis(tribromophenoxy)ethane/Sb_2O_3; epoxylaminate/TBBA; PBT/TBBA; polycarbonate/TBBA; polyurethane/tetrabromophthalic anhydride; polyester/polybrominated polystyrene; polypropylene/dibromopropyldian[b]/Sb_2O_3; ABS/1,2-bis(tetrabromophthalimido)ethane/Sb_2O_3; polystyrene/hexabromocyclododecane	DIN, BIS, VCI[c]; 600°C and 800°C
Dumler, 1989c	Br_{10}DPE; PBT/Br_{10}DPE/Sb_2O_3	VCI[c]; various temps in range 300-800°C; 10 min.
Dumler, 1990	Br_{10}DPE; Br_{10}DPE/Sb_2O_3; PBT/Br_{10}DPE; PBT/Br_{10}DPE/Sb_2O_3	VCI[c]; 300-800°C at 100°C intervals; 10 min.
Hutzinger, 1989	2-bromophenol; 2,4,6-tribromophenol; pentabromophenol; Bromkal 70-5DE (Br_5DPE); HIPS/Br_{10}DPE; ABS/Br_8DPE; polyurethane/Br_5DPE; epoxylaminate/TBBA; polystyrene/hexabromocyclododecane	DIN, BIS, VCI[c]; 600°C for flame retardants, 800°C for polymers. Mass burner (HIPS/Br_{10}DPE only).
Luijk, 1991	Br_5DPE; Br_8DPE; Br_{10}DPE; HIPS/Br_{10}DPE/Sb_2O_3	Sealed vials; 500°, 600°C (PBDPEs only). Tube reactor with N_2 or air flow; various temps in range 275-860°C.
Luijk, 1992	PBT/decabromobiphenyl; ABS/TBBA	Tube reactor with N_2 or N_2/O_2 flow. 400°, 500°, 600° and 700°C.

TABLE 3 (cont.)

O'Keefe, 1978	Firemaster FF-1 (mainly hexabromobiphenyl)	Open tubes and tubes sealed under nitrogen; 380-400°C; 20 min.
Pinkerton, 1989	HIPS/Br_{10}DPE/Sb_2O_3	Mass burner (500-800°C from flame tip to 6" above flame).
Striebich, 1991	2,4,6-tribromophenol; 1,2-bis(tribromophenoxy)ethane; PBDPEs	STDS[d]
Thies, 1990	TBBA; ABS/TBBA/Sb_2O_3; PBT/TBBA/oligocarbonate/Sb_2O_3; TBBA-bisphenol A-copolycarbonate; ABS/TBBA-bisphenol A-copolycarbonate blend	BIS (20 min.), DIN (10 min.)[c]; 600°C
Thoma, 1986a	2,4,6-tribromophenol; pentabromophenol; TBBA; tetrabromophthalic anhydride	Open quartz tubes; 700°, 800°, 900°C; 10 min.
Thoma, 1987a	Bromkal 70 DE (Br_4/Br_5DPE); Bromkal 70-5-DE (Br_5DPE); Bromkal G1 (Br_5DPE); FR 300 BA (Br_{10}DPE); Firemaster BP-6 (hexabromobiphenyl); mixtures of these fire retardants with polystyrene and polyethylene	Open quartz tubes; 700°, 800°, 900°C; 10 min.
Thoma, 1987d	2,4,6-tribromophenol; pentabromophenol; Bromkal 70-5-DE (Br_4/Br_5DPE); FR 300 BA (Br_{10}DPE); Firemaster BP-6 (hexabromobiphenyl)	SGE pyrojector[e]; 600°, 700°, 800°, 900°C

ABS - acrylonitrile/butadiene/styrene copolymer; HIPS - high-impact polystyrene; PBT - polybutylene terephthalate; TBBA - tetrabromobisphenol A
See Table 2
DIN, BIS and VCI - types of apparatus designed to allow heating of a sample in a quartz tube while maintaining a flow of air over the sample, and collection of the volatiles.
System for Thermal Diagnostic Studies. Pyrolysis in the vapour phase in an air or nitrogen stream with a residence time of ca. 2 sec. in the heated zone.
Pyrolysis in He atmosphere with a short residence time in the heated zone.

Br_4DF. Weak signals for the molecular ion isotopes of Br_4DF were also apparent in the low-resolution direct probe mass spectrum of the pyrolisate obtained from Firemaster FF-1 under a nitrogen atmosphere.

Much higher levels (ca. 2000 ppm) of PBDFs were found (Thoma, 1987a) when Firemaster BP-6 (mainly hexabromobiphenyl with ca. 10% heptabromo) was pyrolyzed in an open tube at higher temperatures (700, 800, 900°C) and congeners containing two to seven bromines (maximum at four) were found. In contrast, when pyrolysis was conducted in a helium atmosphere, no PBDFs were detected in the pyrolysate (Thoma, 1987). The results of these studies are consistent with the expectation that oxygen is essential in the formation of PBDFs from polybrominated biphenyls. The highest levels of PBDFs were obtained (Thoma, 1987a) when mixtures of Firemaster BP-6 with polyethylene or polystyrene were pyrolyzed in an open tube (ca. 8000 and 43000 ppm respectively at 700°C). In these cases, only mono- to tetrabromo congeners were found, indicating that debromination reactions are enhanced by the polymers, and the temperature of maximum formation of PBDFs is lower than for Firemaster BP-6 by itself.

In a study of the volatile pyrolysates produced from a PBT/decabromobiphenyl blend under a range of conditions, a maximum yield of ca. 70 ppm Br_4-Br_8DFs was obtained at 600°C in a stream of N_2/O_2 (9:1). Yields of PBDDs were at least two orders of magnitude lower (Luijk, 1991).

The pyrolysis of the polybrominated phenols in the presence of air has been found to give both PBDDs and PBDFs (Hutzinger, 1989; Striebich, 1991; Thoma, 1986a,1989), the levels found being dependent upon the experimental conditions. Particularly high levels of Br_4DDs (up to 9% by weight of the starting phenol) were obtained from 2,4,6-tribromophenol. Much smaller quantities, or none, of these products were found when the pyrolysis was carried out in the absence of oxygen, with apparently complete destruction of brominated products occuring in the vapour phase at temperatures of about 800°C (Striebich, 1991). The derivative 1,2-bis(2,4,6-tribromophenoxy)ethane alone behaved similarly to 2,4,6-tribromophenol (Striebich, 1991), and pyrolysis in air of an ABS copolymer sample containing this compound and Sb_2O_3 as fire retardants gave ca. 1000 ppm PBDFs and ca. 100 ppm PBDDs depending upon the conditions of pyrolysis (Dumler, 1989b).

The largest number of reports in this area concern studies of the pyrolysis of PBDPEs [estimated annual production in Europe of 4500 tonnes (Zier, 1991)] and of polymeric materials containing them. Commercial fire retardant chemicals consisting of mainly Br_4/Br_5DPE (Brombal 70 DE), Br_5DPE (Brombal 70-5-DE, Brombal G1), Br_8DPE or Br_{10}DPE (FR 300 BA) have been investigated. In general, the average degree of bromination of pyrolysis products from pure PBDPEs increases with the degree of bromination of the starting PBDPE(s) and the yield of PBDD/Fs decreases in the sequence Br_5DPE > Br_8DPE > Br_{10}DPE. This reflects the easier ring closure from HBr elimination than from Br_2 elimination (Luijk, 1991).

Pyrolysis of Br_4/Br_5DPE or Br_5DPE in air has been reported (Buser, 1986b; Thoma, 1987a; Hutzinger, 1989; Luijk, 1991; Striebich, 1991) to give a combined yield of PBDDs and PBDFs of from 0.15% for pyrolysis in the vapour phase (Striebich, 1991) to ca. 90% for pyrolysis in quartz tubes (Thoma, 1987a) at or near the optimum temperature for PBDD/F formation under the experimental conditions employed. As would be expected, PBDFs, but little or no PBDDs, were found when pyrolysis was carried out in the absence of oxygen (Thoma, 1987d; Striebich, 1991). Pyrolysis in air of Brombal 70-5-DE in mixtures with polyethylene or polystyrene gave only PBDFs in concentrations similar to those obtained from the fire retardant alone (Thoma, 1987a). PBDD formation is suppressed, apparently because the polymer competes effectively for available oxygen. Considerably reduced quantities of PBDFs and only small amounts of PBDDs were obtained when polyurethane, containing Br_5DPE as flame retardant, was pyrolyzed under similar conditions (Hutzinger, 1989).

Pyrolysis of Br_8DPE (quartz vials, ca. 500-600°C) gave ca. 5% PBDD/Fs (Buser, 1986b; Luijk, 1991), while significantly lower levels (10-200 ppm depending upon apparatus used) were obtained when the flame retardant was incorporated into an acrylonitrile-butadiene-styrene copolymer (Hutzinger, 1989; Dumler, 1989b).

Levels of up to 1-2% of PBDD/Fs have been obtained with pyrolysis of Br_{10}DPE in air (Buser 1986b; Dumler, 1989c, 1990; Luijk, 1991; Thoma, 1987a, 1987d). Pyrolysis of commercial polymer samples, containing Br_{10}DPE as fire retardant, or of synthetic mixtures

of polymer and Br_{10}DPE, can give significantly higher amounts of PBDFs (up to 16% based on Br_{10}DPE content) with only small amounts of PBDDs (Bienieck, 1989; Dumler, 1989a, 1989b, 1989c, 1990; Hutzinger, 1989; Luijk, 1991; Thoma, 1987a). The product mixtures in such cases consist of more lower brominated congeners than are obtained from Br_{10}DPE alone, and the temperature of maximum formation of PBDFs is also lower (500-600°C vs 800°C). Studies of the influence of Sb_2O_3 and polymer separately indicate that the former promotes the formation of PBDFs without changing the pattern of congeners formed, while the latter promotes both debromination and PBDF formation (Dumler, 1990). It has been suggested (Luijk, 1991) that radicals generated by depolymerization of the polymer abstract Br atoms from the Br_{10}DPE. In this study, it was found that heating HIPS/Br_{10}DPE/Sb_2O_3 at 275°C (below the ceiling temperature of the polymer) for 20 minutes gave mainly the higher brominated PBDFs (4.3% based on Br_{10}DPE content). In contrast to the results obtained in pyrolysis experiments, relatively low levels of PBDFs (95% mono- to tribromo congeners), and no PBDDs, were found in the combustion products from a HIPS/Br_{10}DPE/Sb_2O_3 sample (Pinkerton, 1989).

Up to 1600 ppm of PBDD/Fs, consisting mainly of mono- to tribromo congeners were obtained upon pyrolysis of tetrabromobisphenol A (Thoma, 1986a; Thies, 1990), while polymers containing TBBA (or the derived dibromopropyldian - see Tables 2 and 3) gave much lower amounts (ppb up to ca. 40 ppm) of these products under the same conditions (Dumler, 1989b; Hutzinger, 1989; Luijk, 1992; Thies, 1990).

No PBDD/Fs were detected in the pyrolysate (in air) from tetrabromophthalic anhydride (Thoma, 1986a), and only very low levels of mono- to tribromo congeners were obtained from polymers containing it, the related 1,2-bis(-tetrabromophthalimido)ethane, or hexabromocyclododecane (Dumler, 1989b; Hutzinger, 1989). Br_4DDs and Br_4DFs were found in pyrolysates from 2,4,6-tribromoaniline and the related N-(tribromophenyl)maleimide (Alsabbagh, 1992).

2.3 WASTE INCINERATORS

Various authors report the presence of BCDDs and BCDFs in fly ash from commercial waste incinerators (Hosseinpour, 1989; Huang, 1992; Schwind, 1988; Sovocool, 1989; Tong, 1991b), in emissions from municipal and hazardous waste incinerators (Oberg, 1987; Oehme, 1987), in solid material collected from the chimney of an industrial waste incinerator (Schäfer, 1986), and in ash samples from several types of combustion and incinerator processes (Harless, 1989).

Due to the large number of possible PBDD/F congeners (Table 1), a lack of suitable analytical standards, and the complexity of the mixtures of organic compounds produced upon incineration of waste materials, identification and reliable quantitation of specific congeners has, in most cases, not been possible. In one study (Scheind, 1988) of fly ash from a municipal waste incinerator, which was analyzed for all possible congener groups of BCDDs and BCDFs, values estimated for dioxin and furan contents for individual congener groups ranged from 90 to 2131 ppt and 16 to 250 ppt, respectively. A complete series of

tetrahalogenated dibenzofurans ($Br_xCl_{4-x}DF$, x = 0-4) was also detected for the first time.

On more recent work on municipal waste incinerator fly ash (Huang, 1992; Tong, 1991b), representatives of all possible congener groups $BrCl_xDD/F$ (x = 3-7) and Br_2Cl_yDD/F (y = 2-6) were found. Estimated levels for the different monobromo congener groups (Tong, 1991b) ranged from 4 to 17 ppb for dioxins and 1 to 20 ppb for furans for one sample (ca. 4% of the levels of the PCDD/F analogues). Lower levels (6.4 to 981 ppt) were found for the dibromo congener groups in four samples from different incinerators in the U.S. and Canada (Huang, 1992). The finding that the monobromo congeners are more abundant than the more highly brominated species, but less abundant than the PCDD/Fs, is in accord with the expected lower input of bromine sources than of chlorine sources to the incinerator (Buser, 1987b).

In these studies, it was noted that a number of isomers detected in each congener group was low compared to that theoretically possible (even allowing for incomplete GC separation) and that the GC peak pattern observed for each $BrCl_xDD$ or $BrCl_xDF$ congener group seems to be closely related to the peak pattern of the corresponding $Cl_{x+1}DD/F$ congener group. Since all the possible isomers of the PCDD/Fs are believed to be present in municipal waste incinerator fly ash (Karasek, 1986; Tong, 1986), these observations indicate that there is some specificity involved in the formation of the bromo derivatives. It has been suggested (Huang, 1992) that these derivatives may be formed by bromination, in the cooler parts of the incinerator, of preformed PCDD/Fs, if it can be assumed that

bromination in the hottest regions is reversible due to the reactivity of C-Br vs C-Cl bonds.

A number of other studies are of relevance in connection with the possible modes of formation of BCDD/Fs in incinerators. Pyrolysis (open quartz tube) of PBDD/Fs, and of other brominated aromatic derivatives, in the presence of a chlorine source (eg. HCl, NaCl, polyvinyl chloride) has been found to give products of exchange of chlorine for bromine, including products of complete exchange (Thoma, 1987b, 1987c, 1989). Similar chlorine-for-bromine exchange was observed (Zier, 1991) when brominated aromatic compounds, including 2,3,7-Br_3DD and 1,2,3,4-Br_4DD, were heated at 300°C under nitrogen after deposition on fly ash from a municipal waste incinerator. It is suggested that halogen exchange occurs via an ionic mechanism involving nucleophilic displacement of bromide by chloride present in the fly ash, and that such a process may account for the observed increase in output of PCDD/Fs from a municipal waste incinerator when brominated compounds were added to the feed stock.

2.4 MOTOR VEHICLE EMISSIONS

Additives such as 1,2-dibromoethane, bromoethane, and 1,2-dichloroethane have been used at the 0.1 g/L level as scavengers in leaded fuels. Gasoline sales figures for 1988 indicate that of a total of 846 million m^3 sold worldwide, 309 million m^3 were of leaded gasoline (Bacher, 1991). Since the de novo synthesis of PCDD/Fs, and other chlorinated aromatic derivatives, in oxygen-deficient flames appears to be well-established (Ballschmiter, 1983; Crummett, 1984), it might be expected (Buser, 1987b) that compounds of these types, and

bromine-containing analogues, could be generated in the course of combustion of gasolines containing halogenated additives. Indeed, PCDD/Fs have been found in the exhausts of motor vehicles run on leaded gasoline (Bingham, 1989; Marklund 1987, 1990), in exhaust pipe soot (Buchert, 1991), and engine oil (Ballschmiter, 1986). Two groups (Bacher, 1991; Haglund, 1988) have reported finding brominated analogues.

Br_2DF, Br_3DD/F, Br_4DD/F and Br_5DF were detected in the exhaust from a car run on leaded gasoline (Haglund, 1988). Br_2DF was the major component, the amounts of more highly brominated congeners decreasing sharply with increasing bromine content (1,100 ng/km for Br_2DF to 0.98 ng/km for Br_5DF), and the PBDF content of the emissions greatly exceeded the PBDD content. In the more recent study (Bacher, 1991), the whole exhaust stream from a one-cylinder gasoline engine fuelled with isooctane spiked separately with 1,2-dichloro-, 1,2-dibromo-, and 1-bromo-2-chloroethane, was analyzed. These additives resulted in the formation of PCDD/Fs, PBDD/Fs and mainly BCDD/Fs, respectively. The lower halogenated congeners (mono- to tetra-) dominated in these experiments, the amounts formed decreasing sharply from mono/di- to tetra-, with furans predominating over dioxins. The results of these experiments provide clear evidence for the de novo synthesis of halogenated dioxins and furans during combustion. In addition, good agreement was found between the isomer profiles observed for these emissions, and those obtained from certain environmental samples (dust from a highway tunnel and from a public parking garage) which were expected to have a major input from automobile traffic.

3.0 ANALYTICAL METHODOLOGY

In general, analytical procedures developed originally for the PCDD/Fs have been applied, with appropriate modification, to the analysis of the chemically and physically similar PCDD/Fs and BCDD/Fs. For complex samples, the procedures involve:

(i) dissolution or extraction of the sample,

(ii) cleanup (usually chromatographic) of the resulting extracts to remove chemical interferences,

(iii) concentration of the cleaned-up extracts, and,

(iv) separation, identification and quantitation of the target analytes.

The last step is usually carried out using combined gas chromatography/mass spectrometry (GC/MS). Table 4 outlines the USEPA-approved procedures (RCRA Method 8280 and CERCLA IFB WA 86 K-357) for the analysis of PCDD/Fs (Donnelly, 1990a).

Details of the analytical procedures which have been used for PBDD/Fs and BCDD/Fs are summarized in Table 5. In many cases, reliable quantitative results have not been obtained due to a lack of suitable analytical standards, particularly of ^{13}C-labelled derivatives, to allow determination of the efficiency of recovery of analytes during extraction and cleanup, and of relative response factors (RRFs) for quantitation by MS. Additional problems result from;

TABLE 4

Outlines of RCRA Method 8280 and CERCLA Method IFB WA 86 K-357 for the Analysis of PCDDs and PCDFs

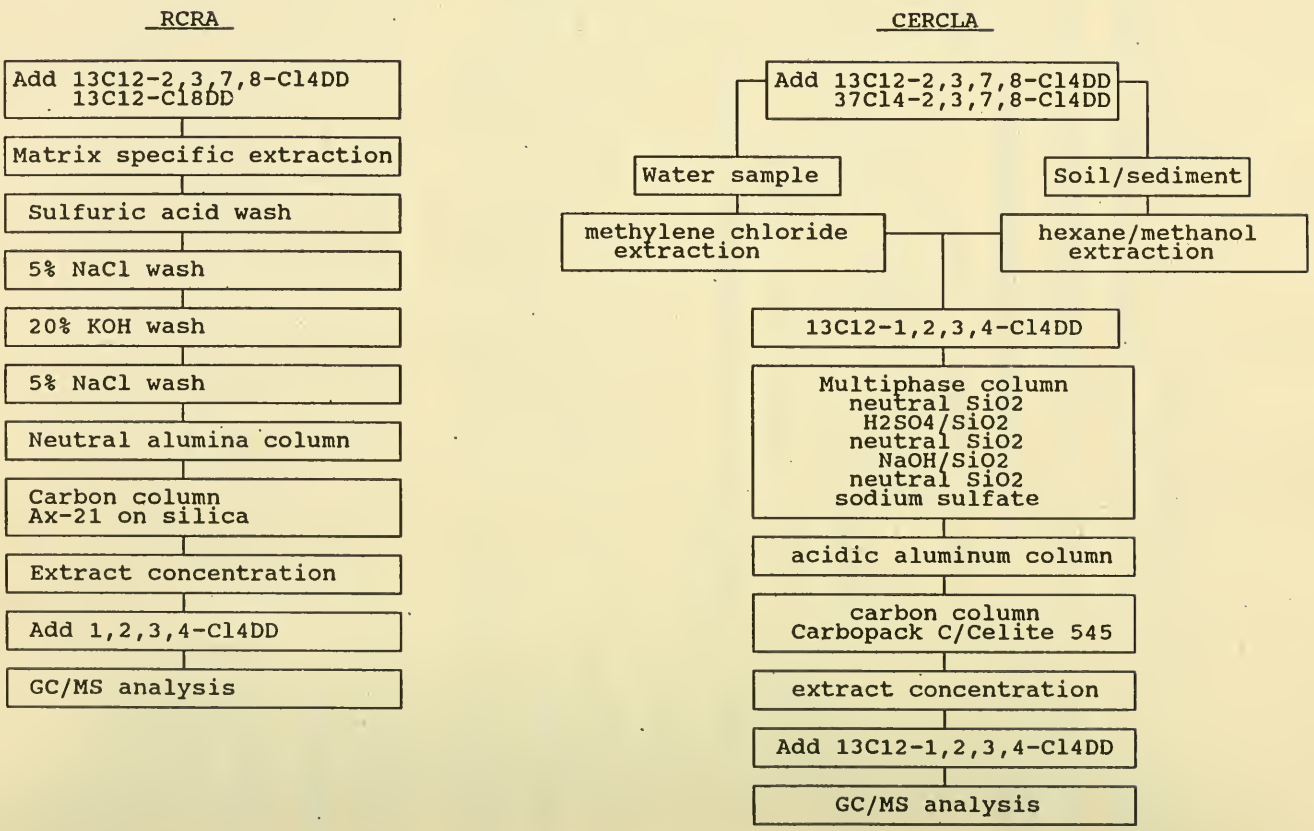


TABLE 5

Conditions Used for the Characterization and Analysis of PBDDs, PBDFs, BCDDs and/or BCDFs in Various Matrices

Publication	Matrix	Extraction	Cleanup	Gas Chromatography	Mass Spectrometry
Alsabbagh, 1992	Pyrolysates from 2,4,6-tribromoaniline and N-tribromophenylmaleimide	Benzene	None	HP5890; 50 m x 0.3 mmid x 0.33 μm film DB5; 70°C (2 m) 7°/m 230°C (5 min) 3°/m 250°C (5 m) 4°/m 295°C (35 m)	MS 5970; SIM
Bacher, 1991	(i) Exhaust from gasoline engine fuelled with isooctane spiked with 1,2-dibromo-, 1,2-dichloro-, or 1-bromo-2 chloro-ethane. (ii) Particulate samples from highway tunnels and underground public garage. (iii) Air sample from underground public garage.	Cited K. Ballschmiter et al, Fresenius Z. Anal. Chem., 1985, 320, 711-717 and 1987, 328, 639-643.		Cited K. Ballschmiter et. al., Fresenius Z. Anal. Chem., 1988, 331, 821-4 and 1989, 333, 744-5.	
Bieniek, 1989	Pyrolysates from PBT/Br_{10}DPE/Sb_2O_3 at various temperatures	No details	Chromatography on various adsorbents (Florisil, Al_2O_3); hexane/CH_2Cl_2 eluant	HRGC - no details	SIM - no details
Buser, 1986a	(i) Products of reaction of 2,3,7,8-Cl_4DD and 2,3,7,8-Cl_4DF with Br_2 in CCl_4. (ii) Pyrolysates from PBDPEs. (iii) Extract of sample from accidental fire.	Dissolve in toluene	None	25 m x 0.31 mmid SE 54; 80°C (2 m) 2°/m 160°C 5°/m 280°C, or 80°C (2 m) 20°/m 180°C 10°/m 280°C	Finnigan 4000; NCI (CH_4, 0.31 torr, 140°C)
Buser, 1986b	Pyrolysates from PBDPEs	Dissolve in toluene	None	25 m x 0.31 mmid x 0.15 μm film SE 54, or 8 m x 0.1 μm film SE 54; 80°C (2 m) 20°/m 180°C 5°/m 280°C (hold)	Finnigan 4000; EI (50 eV)
Buser, 1987a	Mixtures of BCDD/Fs from irradiation of PCDDs/Fs in 1,2-dibromoethane	Dissolve in toluene	None	25 m SE 54; 80° 20°/m 180°C 5°/m 280°C, or 60 m SP2340; 80°C 20°/m 160°C 4°/m 260°C	EI or NCI

TABLE 5 (cont.)

Buser, 1988	Products of photolysis of PBDD/Fs and BCDD/Fs in hydrocarbon solution and on quartz surfaces	Isooctane	None	Carlo Erba Mega; 25 m x0.32 mmid SE 54; 80°C (2 min) 20°/min 160°C 5°/min 300°C (hold)	Finnigan 4000; EI (50 eV); MID
Cramer, 1990	Human adipose tissue samples spiked with Br_4-Br_6DD/Fs	Dissolve in hexane	Treatment with SiO_2/H_2SO_4 slurry followed by chromatography on SiO_2/H_2SO_4, SiO_2, neutral Al_2O_3, and 5% AX-21/SiO_2	Carlo Erba MFC 500; 30 m x 0.25 mmid x 0.25 μm film DB-5; 200°C (2 min) 5°/min 330°C	Kratos MS-50TC; mass resolution 3000
Donnelly, 1987	Br_1-Br_8DD/Fs from $FeBr_3$-catalyzed bromination of DD and DF	RCRA Method 8280 (see Table 4)		30 m x 0.32 mmid x 0.25 μm film DB-5; 170°C (10 min) 8°/min 320°C	Finnigan MAT 4021; EI (70 eV); NCI and PCI (CH_4, 0.3 torr, 100°, 140°, 250°, 270°C)
Donnelly, 1989a	(i) PBT/Br_{10}DPE (ii) HIPS/Br_{10}DPE (iii) ABS/Br_{10}DPE (iv) Pyrolysate from PBT/Br_{10}DPE (v) Fumes from extrusion of resin	(i) Trichloroethane /phenol (soxhlet), then water partitioning of phenol. (ii)-(v) Toluene or CH_2Cl_2 (soxhlet)	Acid and base washes. Chromatography on multiphase silica, acidic Al_2O_3, and two successive carbon columns.	30 m x 0.25 mmid x 0.25 μm film DB-5, or 30 m x 0.25 mmid x 0.25 μm film SPB-5 (Supelco)	Finnigan 4023 (low resolution); VG 7070EQ and VG 70-250SE; EI (70 eV); SIM
Donnelly, 1989b	Synthetic BCDD/F mixtures spiked on sand	RCRA Method 8280 (see Table 4)		30 m DB-5; 175°C (1 min) 4°/min 320°C; 175°C (10 min) 8°/min 320°C	EI (70 eV)
Donnelly, 1990b	Synthetic BCDD/Fs	-----	-----	-----	Finnigan 4021; EI (70 eV); full scan mode (table of relative ion abundances for specific isomers)
Donnelly, 1990c	(i) ABS/PBDPE (ii) Municipal waste incinerator fly ash (iii) Polyethylene terephthalate/PBDPE (iv) HIPS/PBDPE (v) Automotive fluff waste (vi) PBT/PBDPE	(i) CH_2Cl_2 (reflux) (ii)-(v) Benzene or toluene (soxhlet) (vi) Trichloroethane /phenol (reflux)	Chromatography on multiphase SiO_2, acidic Al_2O_3, then 5% AX-21/SiO_2 (two columns if high PBDPE), or HPLC on 5% AX-21/10 μm SiO_2	30 m x 0.25 mmid x 0.25 μm film DB-5; 170°C (1 min) 5°/min 320°C	Finnigan 4023 (low res); EI (70 eV). VG 7070EQ or VG-250SE (high res); EI (70 eV); full scan and SIM modes.

TABLE 5 (cont.)

Donnelly, 1991a	Synthetic PBDD/Fs (development of retention index model)	-----	-----	HP5880A; 30 m x 0.25 mmid x 0.25 μm film RTx-5 with FID; 170°C (1 min) 2°/min 320°C	EI; full scan mode; same or faster (4°/min) temp. program as for FID
Donnelly, 1991b	Synthetic PBDD and BCDD mixtures (retention index determinations)	-----	-----	As above.	-----
Donnelly, 1991c	Commercially available standards and synthetic mixtures of PBDD/Fs and BCDDs (development of a retention index model)	-----	-----	As above for PBDDs and BCDDs, or HP5890; 60m x 0.25 mmid x 0.25 μm film RTx-5; 170°C 1°/min 320°C for PBDFs	----- VG 70-250SE; EI
Dumler, 1989a and 1989c	Pyrolysates from Br_{10}DPE and samples of PBT/Br_{10}DPE/Sb_2O_3 (collected on XAD-2)	Toluene	Chromatography on H_2SO_4/SiO_2 and $NaOH/SiO_2$ (hexane eluant)	12.5 m Ultra 2; 100°C (1 min) 20°/min 180°C 5°/min 320°C (7 min)	HP GC/MSD; EI; SIM
Dumler, 1989b	Pyrolysates from various polymers containing brominated flame retardants	Toluene (soxhlet, 48 h)	Wash with H_2SO_4, then chromatography on multilayer SiO_2/H_2SO_4 and $NaOH/SiO_2$ (hexane eluant)	As above.	As above.
Dumler, 1990	Combustion products from Br_{10}DPE, PBT/Br_{10}DPE, Br_{10}DPE/Sb_2O_3 and PBT/Br_{10}DPE/Sb_2O_3 (collected on XAD-2)	Toluene (soxhlet)	Chromatography on H_2SO_4/SiO_2 and $NaOH/SiO_2$ (hexane eluant).	As above.	As above.
Haglund, 1988	Vehicle exhaust from: (i) car fuelled with leaded gasoline, (ii) car fuelled with unleaded gasoline, and, (iii) heavy duty diesel truck.	Cited U. Stenberg et. al., Environ. Health Perspect., 1983, 47, 43-51.	Chromatography on SiO_2 (hexane), H_2SO_4 extraction, chromatography on H_2SO_4/Chromosorb, Al_2O_3 and charcoal on Chromosorb	25 m x 0.2 mmid x 0.33 μm film SE 54; 180°C (3 min) 30°/min 240°C 5°/min 300°C (20 min)	Finnigan 4021; NCI (CH_4, 0.4 torr, ca. 80°C).
Harless, 1989	Ash samples from various types of incineration processes	Benzene (soxhlet)	Chromatography on Al_2O_3 and carbon	30 m SE 54, or 60 m SP 2331	Varian MAT 311A; EI; SIM; mass res. 8000-10000

TABLE 5 (cont.)

Hileman, 1989	PBDPEs	Dissolve in CH_2Cl_2/hexane (1:3) (Br_{10}DPE only partly soluble)	Chromatography on two successive 18% Carbopak C/Celite columns	30. m x 0.32 mmid x 0.25 μm film DB-5	HP 5985B; EI (70 eV); SIM
Hosseinpour, 1989	(i) Synthetic BCDDs (ii) Fly ash from municipal waste incinerator	(ii) Wash with 10% HCl then water; dry and extract with toluene (soxhlet)	(i) RP-HPLC; Bischoff 4025, ODS II, 5 μm, 24 cm x 4 mmid, MeOH eluant (ii) Chromatography on multiphase SiO_2, then active Al_2O_3	HP5890; 25 m x 0.2 mmid x 0.33 μm film Ultra 2; 100°C (1 min) 20°/min 180°C 5°/min 320°C (15 min)	HP MSD 5970B; EI (70 eV); SIM
Huang, 1992	Fly ash from municipal waste incinerator	Soxhlet extraction, acid/base wash and multicolumn fractionation as for PCDDs. See H.Y. Tong et. al., Chemosphere, 1989, 18, 577 and L.Q. Huang et. al., Biol. Mass Spectrom., 1991, 20, 161.		HP 5890; 60 m x 0.32 mmid x 0.25 μm film DB-5; 200°C (2 min) 5°/min 220°C (16 min) 5°/min 235°C (7 min) 5°/min 330°C (5 min)	Kratos CONCEPT IS; EI (30-40 eV); tuned for res. >10000 at 10% valley definition; HRSIM
Hutzinger, 1989	Pyrolysates from: (i) bromophenols, Bromkal 70-5DE, and, (ii) various fire-retardant-containing polymer samples	Toluene. Extracts from (i) examined directly by GC/MS.	(ii) H_2SO_4 wash followed by chromatography on multiphase KOH/SiO_2 and H_2SO_4/SiO_2 (n-hexane eluant)	12 m x 0.2 mmid x 0.33 μm film SE 54 fused silica; 100°C (1 min) 20°/min 180°C 5°/min 300°C (12 min)	HP GC/MS; SIM
Luijk, 1991	(i) Pyrolysates from Br_5DPE, Br_8DPE and Br_{10}DPE (ii) Pyrolysate from HIPS/Br_{10}DPE/Sb_2O_3	(i) Toluene and hexane (ii) Toluene and ethanol	(i) Chromatography on $AgNO_3$, neutral and basic SiO_2, and Al_2O_3 (ii) Acid and base washes, then chromatography on Al_2O_3 and multiphase SiO_2	HP 5890; 20 m or 60 m x 0.32 mmid x 0.25 μm film DB-5; 140°C 40°/min 200°C 8°/min 325°C	HP 5970B; EI (70 eV); SIM
Luijk, 1992	Volatile pyrolysates from PBT/decabromobiphenyl and ABS/TBBA	Hexane and methanol washes	Chromatography on carbon and multiphase SiO_2	30 m x 0.32 mmid x 0.25 μm film DB-5; 160°C 40°/min 200°C 8°/min 320°C (30 min)	Kratos CONCEPT 2; SIM
Lutes, 1992a, 1992b	(i) Air samples containing combustion products from polyurethane foam treated with Br_4-Br_5DPEs before and after aging in sunlight (ii) Products from photolysis of Br_4-Br_6DPEs coated on Teflon-impregnated glass fibre filters	Toluene (soxhlet)	Chromatography on acidic SiO_2, Florisil and 7.9% AX-21/Celite	HP 8290; 30 m x 0.32 mmid DB-5	VG 70-250EQ; SIM; resolving power 10,000 (10% valley definition)

TABLE 5 (cont.)

McAllister, 1990	Commercial samples of HIPS/Br_{10}DPE/Sb_2O_3, PBT/Br_{10}DPE/Sb_2O_3, and ABS/Br_8DPE/Sb_2O_3 after processing under normal or 'abusive' thermal conditions	Grind to powder (in liquid nitrogen-cryogenic grinder) and extract with hexane (soxhlet)	Chromatography on SiO_2, Al_2O_3 and carbon	HRGC (no details given)	HRMS (no details given)
Munslow, 1987	Br_1-Br_8DDs from $FeBr_3$-catalyzed bromination of DD in CCl_4 (retention index determinations)	Dissolve in toluene	——	30 m x 0.32 mmid x 0.25 μm film DB-5; 170°C (1 min) 2°/min 340°C	Finnigan 4023; EI (70 eV)
Munslow, 1989	Synthetic BCDDs	Dissolve in benzene	Wash with 10% KOH to remove phenolic residues from syntheses	As above, but with temp. program 170°C (1 min) 6°/min 320°C	As above.
Nestrick, 1989	Synthetic ^{13}C-labelled Br_1-Br_3DD/Fs	Dissolve in hexane	Multicolumn chromatography to remove hydrocarbon contaminants. Separation by RP-HPLC (ODS/Zorbax) then NP-HPLC (Ro-Sil)	20 m x 0.17 mmid x 0.25 μm film DB-5; -65°C (1 min) 30°/min 155°C 5°/min 285°C (hold)	HP 5987A (operating at unit resolution); EI; full scan and SIM
Neupert, 1989a	(i) 2,3,7,8-Br_4DD in arachidis oil, (ii) Faeces, liver or adipose tissue from rats to which (i) had been administered	(ii) Homogenize with solid Na_2SO_4 and elute with hexane/CH_2Cl_2 (1:1)	(i) Chromatography on Al_2O_3 (ii) Chromatography on multiphase SiO_2 then Al_2O_3	HP 5890; 25 m x 0.32 mmid Ultra 1	HP MSD 5970
Neupert, 1989b	(i) Pyrolysis gas condensate from ABS/Br_8DPE/Sb_2O_3 (ii) Tissue from rats to which (i) had been administered	(i) Dissolve in toluene/hexane (1:1) (ii) See (ii) above.	(i) Chromatography on multiphase SiO_2, carbon and Al_2O_3 (ii) See (ii) above.	HP 5890; 25 m x 0.32 mmid Ultra 1; 70°C (2 min) 10°/min 325°C (2.5 min). Also 22 m x 0.32 mmid RTx 2330 (Restek) or 12 m x 0.2 mmid SB-SMECTIC (Lee Scientific)	HP MSD 5970
Oberg, 1987	Flue gas samples from a hazardous waste incinerator collected in probe with filter, condensate collector and XAD-2	No details	Aqueous wash (pH 12) then HPLC on 25 cm x 4.6 mm Spherisorb A54	60 m x 0.25 mmid x 0.25 μm film DB-5, or 60 m x 0.25 mmid x 0.25 μm film SP2331	EI; SIM

TABLE 5 (cont.)

Oehme, 1987	Flue gas samples from six municipal waste incinerators (filter, condenser and XAD-2 trap)	Toluene (soxhlet)	Chromatography on Florisil then HPLC on 25 cm x 4.6 mm Nucleosil 5 μm NO_2- Carbon column for dirty samples	30 m x 0.3 mmid x 0.15 μm film SE 54, or 30 m x 0.25 mmid fused silica SP2330	EI or NCI; SIM
O'Keefe, 1978	Pyrolysis residues from Firemaster FF-1 (mainly hexabromobiphenyl)	Benzene	Chromatography on sodium carbonate, graphitized charcoal and activated Al_2O_3	-----	AEI MS9; EI (70 eV); direct probe
Ramalingam, 1986	Synthetic PBDDs, BCDDs and Br_4DFs	-----	-----	Varian 3740 with ECD, or Perkin Elmer Sigma III; 60 m (0.25 μm film) DB-5; 180°C (1 min) 10° or 5°/min 300°C (hold)	Kratos MS 25; EI (70 eV); SIM
Schafer, 1986	Chimney soot from industrial waste incinerator	Toluene/methoxyethanol/HCl (soxhlet)	Chromatography on superactive Al_2O_3	HP 5890; 45 m x 0.2 mmid x 0.2 μm film CP SIL 5, 100°C (5 min) 5°/min 300°C (15 min); or 60 m x 0.2 mmid x 0.15 μm film DB 1701, 140°C (5 min) 3°/min 310°C (15 min)	HP 5970 MSD; full scan and SIM
Schecter, 1991	2,3,7,8-Br_4DD in human blood sample	Homogenized with acetone/hexane, layers separated, and aqueous acetone layer washed with more hexane	Defatted with conc. H_2SO_4	DB17 (J&W) capillary column	ZAB-2F; EI; mass res. 5000
Schimmel, 1992	Waste incinerator fly ash samples	Conc. HCl treatment followed by toluene/methoxyethanol (reflux 18h) then washes with water and 2M K_2CO_3	Sulfur removal by copper amalgam treatment; chromatography on basic Al_2O_3 (superactive)	HP 5890; 60 m x 0.32 mmid x 0.17 μm film SP 2331; 120°C (15 min) 20°/min 180°C 2°/min 250°C	HP 5970; SIM
Schwind, 1988	Municipal waste incinerator fly ash	Wash with 10% HCl then distilled water; dry, extract with toluene (soxhlet)	Chromatography on multiphase SiO_2 followed by active Al_2O_3	HP 5890; 12.5 m x 0.2 mmid x 0.33 μm film Ultra 2; 100°C (1 min) 20°/min 180°C 5°/min 320°C (15 min)	HP MSD 5970B; EI (70 eV); SIM
Sovocool, 1987	Br_1-Br_8DFs from $FeBr_3$-catalyzed bromination of DF in CCl_4	Dissolve in toluene	-----	30 m x 0.3 mmid x 0.15 μm film DB-5; 170°C (1 min) 2°/min 320°C	Finnigan 4023; EI (70 eV)

TABLE 5 (cont.)

Sovocool, 1989	Municipal waste incinerator fly ash	Benzene (soxhlet)	Acid and base washes followed by chromatography on Al_2O_3 and carbon	30 m x 0.32 mmid x 0,25 μm film DB-5; 170°C (10 min) 8°/min 310°C	Finnigan MAT 4023; EI (70 eV), CI; full scan; or VG ZAB-3F; EI; scan mode or SIM
Striebich, 1991	Volatiles from vapour phase pyrolysis of flame retardants	-----	-----	12 m x 0.2 mmid x 0.1 μm film BP-5 (SGE); -60°C 12°/min 300°C	HP 5970B; SIM
Thies, 1990	(i) Air samples (XAD-2) (ii) Off-gas from compounding machine (SiO_2 cartridge) (iii) TBBA (iv) Polymers containing TBBA or its derivatives as flame retardants (v) Pyrolysis gas condensate from TBBA (vi) Condensates and residues from pyrolysis of polymers in (iv)	(i), (ii) Wash with toluene (iii)-(vi) Toluene (reflux 4h or soxhlet)	Chromatography on multiphase SiO_2, carbon and Al_2O_3	(a) 12 m x 0.2 mmid x 0.22 μm film Ultra 1; 100°C (2 min) 15°/min 350°C (b) 12 m x 0.33 mmid x 0.22 μm film Ultra 1; 70°C (2 min) 12°/min 325°C (7.5 min)	(a) Finnigan 4600 (b) HP MSD 5970
Thoma, 1986a	Pyrolysates from flame retardants	Dissolve in toluene	Wash with IN NaOH or IN NaOH then conc. H_2SO_4	HP 5890; 12 m OV1; 100°C (1 min) 20°/min 180°C 5°/min 320°C (20 min)	HP MSD 5970; EI (70 eV); SIM
Thoma, 1986b	Flame retardants	Dissolve in toluene	Chromatography on multiphase SiO_2 and Al_2O_3	As above.	As above.
Thoma, 1987a	Pyrolysates from flame retardants and their mixtures with polyethylene or polystyrene	Dissolve in toluene	Chromatography on SiO_2	12 m x 0.2 mmid x 0.33 μm film SE 30; 100°C (1 min) 20°/min 180°C 5°/min 320°C (12 min)	As above.
Thoma, 1987b	Pyrolysates from mixtures of PVC with 1,2,3,4-Br_4DD, a PBDD/F mixture, or flame retardants	Dissolve in toluene	As above.	As above.	As above.
Thoma, 1987c	Pyrolysates from mixtures of 1,2,3,4-Br_4DD with PVC, HCl or NaCl	Dissolve in toluene	Wash with water	As above.	As above.

TABLE 5 (cont.)

Thoma, 1987d	Pyrolysates from flame retardants (bromophenols, PBDPEs and polybromobiphenyl)	Volatiles directly to GC/MS	-----	HP 5890; 12 m x 0.2 mmid x 0.33 μm film OV1; 100°C (1 min) 20°/min 180°C 5°/min 320°C (10 min)	HP MSD 5970; EI (70 eV)
Thoma, 1989	Residues from pyrolysis of 1,2,3,4-Br_4DD with conc. HCl, NaCl or PVC	Dissolve in toluene	Wash with distilled water, and dry (Na_2SO_4)	12 m x 0.2 mmid x 0.33 μm film SE 30; 100°C (1 min) 20°/min 180°C 5°/min 320°C	As above.
Tondeur, 1990	Flame retardants (i)-(iv) spiked with PBDD/Fs. (i) Br_3DPE (ii) Br_6DPE (iii) Br_{10}DPE (iv) TBBA	(i)-(iii) Dissolve in CH_2Br_2 (iv) Liquid-liquid partition with methanol/hexane/water (5:5:1)	(i)-(iii) Chromatography on multiphase SiO_2, Florisil, and carbon/SiO_2 (twice) (iv) Chromatography on Bondesil™ (prep. grade, 40 μm)	HP 5790; 30 m x 0.25 mmid x 0.25 μm film DB-5; 150°C ballistic ramp 190°C 3°/min 320°C	VG 70S; EI; SIM; mass res. 100 ppm
Tong, 1991a and 1991b	Municipal waste incinerator fly ash	Benzene (soxhlet)	Wash with conc. H_2SO_4 and water. Chromatography on SiO_2, Al_2O_3 and carbon.	Carlo Erba GC; 60 m x 0.32 mmid DB-5; 80°C (2 min) 15°/min 300°C (15 min)	Kratos MS-5D; EI (70 eV); MID; mass profile monitoring mode (sweep width 300 ppm)
Wagel, 1989	2,3,7,8-Br_4DD and 2,3,7,8-Br_4DF from ambient air sampler	Toluene (soxhlet, 16h)	Acid and base washes, then chromatography on multiphase SiO_2, Al_2O_3 and PX-21/Celite 545	Carlo Erba 4200	Kratos MS-25; SIM
Watanabe, 1987	Products of UV or sunlight photolysis of Br_{10}DPE in hexane/benzene/acetone (8:1:1)	-----	-----	HP 5710A; 25 m x 0.32 mmid x 0.25 μm film OV1; 150°C 8°/min 320°C	JEOL JMS DX-300; EI (70 eV)
Zier, 1991	BCDDs from heating washed municipal waste incinerator fly ash spiked with 2,3,7-Br_3DD or 1,2,3,4-Br_4DD	Dichloromethane/benzene (9:1); volatiles collected in hexane/dichloromethane (1:1)	-----	10 m x 0.25 mmid x 0.25 μm film SP2330; 50°C (1 min) 10°/min 247°C	HP 5970B; scan mode; SIM

(i) the very low solubilities of these compounds and their strong retention on the adsorbents used for extract cleanup (especially the higher brominated congeners),

(ii) the photolytic sensitivity of the brominated congeners (see section 4.0), and,

(iii) the large number of theoretically possible congeners, particularly in the case of the BCDDs and BCDFs (see Table 1).

The difficulty which may be involved in obtaining reliable quantitative results is illustrated by the relatively recent report (Remmers, 1991) that all sixteen analytical protocols submitted to date for measurement of PBDD/Fs in brominated aromatic chemicals under the USEPA testing and reporting rule (USEPA, 1987) were judged to be inadequate at the targeted levels of quantitation. In order to share method development and analytical costs associated with responding to the rules for brominated compounds, three companies have formed an industry consortium, the Brominated Flame Retardant Industry Panel (BFRIP). In the course of the development of analytical methods, the BFRIP has produced a retention index system for the identification of analytes for which standard analytical reference materials are not available, and has generated and characterized a heptabrominated dioxin standard.

3.1 EXTRACTION TECHNIQUES

Details of the methods employed vary with the matrix involved; Table 5 should be consulted for specific cases. Aromatic solvents (benzene, toluene) have been used most frequently, followed by hexane, dichloromethane and a 1,1,1-trichloroethane/phenol mixture. The last solvent combination has been recommended as being more efficient than toluene for the extraction of PBT-containing resin samples (Donnelly, 1989a, 1990c). Dibromomethane has been recommended (Tondeur, 1990) as a solvent for PBDPEs, particularly the rather insoluble Br_{10}DPE.

3.2 CLEANUP PROCEDURES

Two groups (Donnelly, 1987; Luijk, 1991) have reported investigations of the efficiency of recovery of PBDD/Fs (one compound from each Br_2-Br_7 congener group) at each stage of cleanup using RCRA Method 8280. In general, satisfactory recoveries (60-120% range) were obtained at each step. A similar study of the extraction and cleanup of synthetic BCDD/Fs spiked on sand gave overall recoveries which were generally in the range 70-100% (Donnelly, 1989b). As a result of an evaluation of the application of the CERCLA and RCRA methods (Table 4) to the analysis of various types of matrices for PCDD/Fs, it was concluded (Donnelly, 1990a) that overall, the best sample cleanup scheme employs the CERCLA multiphase silica and acidic alumina columns followed by the RCRA AX-21 carbon adsorption column. This combination of cleanup steps was used in the analysis of several flame-retardant-treated resins and related samples (Donnelly, 1989a). The accuracy of the revised method was found to be lower in some instances for PBDD/Fs than for the

corresponding PCDD/Fs, and this was associated with poor (<30%) isotopic surrogate recoveries for some samples. (Loss of analytes on glass surfaces during cleanup could be reduced by silanisation of the glassware with Me_2SiCl_2). Problems were also associated with the darkening and considerable heat generated when extracts were washed with concentrated H_2SO_4, and with the precipitation of significant amounts of solid material when initial extracts were washed with water.

Good recoveries of Br_4 and Br_5DD/F (spiked) from adipose tissue samples were obtained (Cramer, 1990) after cleanup by H_2SO_4 extraction followed by chromatography on H_2SO_4/SiO_2, Al_2O_3 and 5% AX-21/SiO_2. Recoveries of Br_6DD/Fs from the samples were much more variable (^{13}C-labelled standards were not available in these cases) and, on average, lower. Acceptable recoveries (50-150%) were reported (Tondeur, 1990) for ^{13}C-labelled Br_4DD/F, Br_5DD/F and Br_6DD internal standards after addition to samples of TBBA, Br_5DPE and Br_8DFE followed by cleanup as indicated in Table 5, but recoveries from Br_{10}DPE ranged from 22% to 43%.

Efficient separation of PBDFs from PBDPEs, which can interfere in subsequent MS quantitation of the PBDFs (see below) has proved difficult, particularly in samples containing large amounts of PBDPEs. Even the use of two successive carbon columns does not eliminate all traces of these compounds (Tondeur, 1990) and care has to be taken to avoid cross-contamination of samples during analysis when relatively large quantities of PBDPEs are being processed. Although greater separation efficiency could be obtained by

using more or larger carbon columns, this would likely be offset by poorer overall recoveries, particularly of the more highly brominated PBDFs whcih tend to be retained tenaciously on carbon (Hileman, 1989).

Ideally, at least one recovery standard is needed for each congener group analyzed. Since only a few such standards are commercially available, PCDD/Fs have often been used as surrogates for PBDD/Fs and BCDD/Fs, and the final quantitation made with the assumption that recoveries are similar. Clearly, the accuracy of such results is questionable.

3.3 GAS CHROMATOGRAPHY/MASS SPECTROMETRY (GC/MS)

Since large numbers of PBDD/Fs, BCDD/Fs (Table 1) and other aromatic derivarives with similar chemical and physical properties, may be encountered in samples undergoing analysis, GC/MS has been the only analytical technique developed for the routine analysis of such compounds. Relatively few standard compounds (^{13}C-labelled or native) being commercially available, several groups have reported syntheses (most commonly of mixtures) of compounds to allow characterization of the GC and MS properties of as wide a range of PBDD/Fs and BCDD/Fs as possible. Because of the high toxicities associated with certain derivatives, these syntheses have usually been carried out on a very small scale with a minimum of purification steps. In a few cases, individual compounds have been purified by HPLC.

PBDD/Fs have most often been prepared by electrophilic bromination of DD (Munslow, 1987) or DF (Hutzinger, 1987; Sovocool, 1987; Tashiro, 1982). A microscale (0.1 μg to 10 mg) procedure for the preparation, from commercially available $^{13}C_{12}$-DD and $^{13}C_{12}$-DF, of ^{13}C-labelled PBDD/Fs containing up to four bromines in the 2-,3-,7- and 8- positions has been described (Nestrick, 1989). PBDFs have also been obtained by palladium acetate oxidation of PBDPEs (Ramalingam, 1986).

Although BCDD/Fs can be obtained by electrophilic bromination of PCDD/Fs (Donnelly, 1989b; Hosseinpour, 1989; Kende, 1973, 1974), γ -irradiation of the latter in 1,2-dibromoethane is reported (Buser, 1987a) to be more convenient and to give better yields for the more highly chlorinated precursors. BCDD/Fs have also been prepared by chlorination of PBDD/Fs (Donnelly, 1989b; Kende, 1973, 1974). Other routes to BCDDs have involved (i) halogen exchange by pyrolysis of PBDDs in the presence of HCl (Schwind, 1988), (ii) thermolysis of the potassium salts of bromochlorophenols (Munslow, 1989), and (iii) reaction of halocatechols with halonitrobenzenes in the presence of base (Donnelly, 1991a; Ramalingam, 1986).

As might be expected, due to their higher molecular weights, the PBDD/Fs and BCDD/Fs have longer GC retention times than the corresponding PCDD/Fs under the same GC conditions. However, the results of GC investigations of synthetic PBDDs (Donnelly, 1987, 1991a, 1991b, 1991c; Munslow, 1987; Ramalingam, 1986), PBDFs (Donnelly, 1991c; Sovocool, 1987), BCDDs (Buser, 1987a; Donnelly, 1989b, 1991a, 1991b, 1991c; Munslow,

1989; Ramalingam, 1986) and BCDFs (Buser, 1987a; Donnelly, 1989b) indicate that, for all four classes, the elution order of isomers within each congener group is very similar to the elution order of isomers in the corresponding PCDD or PCDF congener group. On the basis of this type of information, a GC retention index (RI) model has been devised (Donnelly, 1991a-c) to allow the prediction of RIs for compounds presently unavailable, and to assist in the assignment of structures to isomers whose molecular formula has been established by MS. These RIs have been used for the assignment of structures to BCDDs found in waste incinerator fly ash samples (Donnelly, 1991b; Huang, 1992).

MS is used both for identification of individual analytes after GC separation and for quantitation. Since there are two isotopes of both chlorine (^{35}Cl, ^{37}Cl) and bromine (^{79}Br, ^{81}Br), molecular ions, and most fragment ions, of the PBDD/Fs and BCDD/Fs, appear in the mass spectra as clusters in which the number and relative intensities of the individual components are predictable, and reflect the number and nature of the halogen atoms present. A combination of mass and relative peak intensity measurements of a molecular ion cluster may be used to assign a molecular formula to an analyte separated by GC. Further support for such an assignment can be provided by the fragmentation pattern in the full-scan mass spectrum, if obtainable.

Electron impact (EI) mass spectral fragmentation patterns have been discussed for PBDDs (Buser, 1986b; Donnelly, 1987; Kende, 1973; Munslow, 1987; Nestrick, 1989), PBDFs (Buser, 1986b; Donnelly, 1987; Hutzinger, 1989; Nestrick, 1989; Sovocool, 1987), BCDDs

(Buser, 1987a; Donnelly, 1990b; Kende, 1973; Munslow, 1989) and BCDFs (Buser, 1987a; Donnelly, 1990b). In all cases, except those of 2-BrDF (Sovocool, 1987) and Br_8DF (Hutzinger, 1989), a $M^{+\cdot}$ ion is the base peak. Negative ion chemical ionization (NCI) mass sepctra have been described for PBDD/Fs (Buser, 1986a; Donnelly, 1987) and for BCDD/Fs (Buser, 1987a). In the case of the PBDD/Fs, the spectra are dominated by the $^{79}Br^-/^{81}Br^-$ signals, but the molecular ion clusters are observable, and their relative intensities may be increased by lowering the ion source temperature (Donnelly, 1987; Haglund, 1988). With the BCDD/Fs, relatively strong $M^{-\cdot}$ signals are observed and the intensity of the Br^- signal decreases relative to that of $M^{-\cdot}$ with increasing number of chlorines in the molecule. Positive ion chemical ionization (PCI) mass spectra have also been recorded for some PBDD/Fs (Donnelly, 1987).

While both low and high resolution MS have been used for the analysis of halogenated DD/Fs, the resolving power of combined capillary column GC (HRGC) and high resolution MS (HRMS) is essential for the multicomponent analysis of complex matrices such as waste incinerator fly ash samples. For the detection of analytes as they elute from the GC column, the spectrometer is operated in the selected-ion-monitoring (SIM) mode for maximum sensitivity of detection. The resulting data are used to produce chromatograms. Multiple ion detection (MID) systems allow simultaneous monitoring of several ions, thereby facilitating comparison of peak intensities within ion clusters for the identification of specific analytes, and simultaneous quantitation of several analytes.

Unequivocal identification, and subsequent reliable quantitation, of a specific analyte necessitates the signals ascribed to it be adequately resolved from those of closely-eluting or coeluting compounds. Two types (i and ii below) of interfering compounds may be distinguished:

(i) Certain compounds produce ions of identical molecular formula to those of the analyte. This applies particularly to the various isomers within the different PBDD/F and especially BCDD/F congener groups where complete resolution by GC is unlikely to be achieved, and can prevent the identification and accurate quantitation of highly toxic isomers. PBDPE impurities can interfere in the analysis of PBDFs, since the $[M\text{-}2Br]^{+\cdot}$ fragment of a PBDPE (and lower fragments) has the same mass as the $M^{+\cdot}$ fragment (and lower fragments) of the PBDF with two fewer bromines in the molecule. The possibility of such interference can be checked by concurrently monitoring for the $M^{+\cdot}$ ion of the PBDPE. With HRGC, these compounds do not coelute, but the $[M\text{-}HBr]^{+\cdot}$ fragment from a PBDPE having one more bromine atom than the PBDF may now interfere. Although this fragment does not have greater than 3% relative intensity, high levels of PBDPEs can be present in some samples (Donnelly, 1990c).

(ii) Potentially, a large number of halogenated aromatic derivatives can give ions of the same nominal mass as those most commonly monitored for the analysis of PBDD/Fs or BCDD/Fs. In such cases, it may be possible to select alternative ions for monitoring the analytes of interest. A database of ion masses for halogenated derivatives of DD, DF and other polycyclic aromatic molecules, has been compiled and a computer program devised to allow inter alia selection of appropriate ion masses for SIM of specific analytes and prediction of possible interfering compounds (Beard, 1991). For example, interference with the $M^{+\cdot}$ ion of PBDDs may be caused by the $[M+2]^{+\cdot}$ ion of polybromoxanthenes (Donnelly, 1987, 1989a), and with the $M^{+\cdot}$ ion of PBDFs by the $[M\text{-}Br]^{+\cdot}$ fragment ion of the $^{13}C_1$-PBDPE that contains one more bromine than the PBDF. Although the last fragment has relatively low intensity, again high levels of PBDPEs may be present in some samples.

Recently, for cases where the required MS resolution is at or beyond the limits obtainable by SIM with peak top monitoring, mass profile (MP) monitoring has been shown to offer significant advantages (Tong, 1991a, 1991b, 1992). Examination of mass profile peak shapes, centroid positions, and sequential changes during GC elution, can both reveal the presence of interfering compounds and provide accurate mass measurements for them. To compensate for the loss of sensitivity resulting from operation in the MS vs peak top monitoring mode, the spectrometer can be operated at lower resolution (typically 5000-10000 at 10% valley). At a resolution of 8000, a mass difference of 6 ppm could be detected which corresponds to an interference that would require a mass-resolving power of 170000 for adequate separation by peak top monitoring. The MP method also provides detection limits at the picogram level.

Quantitation of an analyte is accomplished by comparison of the mass spectral response of the analyte in the sample with that of a standard for which the RRF has been measured or estimated. In many cases, standards of specific analytes, or isomers thereof, are unavailable, and synthesis is impractical given the number of possible compounds (Table 1). PCDD/Fs have therfore often been used as surrogates for the PBDD/Fs and BCDD/Fs with the assumption that RRFs are the same for compounds with the same number of halogens in the molecule. Results thus obtained can only be relied upon as being semiquantitative, as is illustrated by the report (Tong, 1991b) that levels of two BCDDs in incinerator ash samples measured using BCDD standards were four times greater than those obtained using PCDD surrogates.

Most analyses have been performed with the MS operating in the EI mode. The NCI technique, while affording high sensitivity by monitoring for Br^-, is less suitable for quantitative analysis because the MS response factors vary with the isomeric substitution pattern, and depend upon many parameters such as reagent gas pressure, source temperature, and trace impurities in the reagent gas (Huang, 1992; Tong, 1991b).

The following GC/MS confirmation criteria have been proposed (Donnelly, 1987, 1989b) for the analysis of PBDD/Fs and BCDD/Fs.

(i) GC retention time, or retention index (RI), must be correct for the analyte of interest.

(ii) Surrogate recoveries must be in the 40% to 120% range.

(iii) All m/z monitored for a given analyte must maximize simultaneously ($\pm$ 1 sec) with a signal-to-noise ratio greater than or equal to 2.5 for each.

(iv) The ratio between pairs of ions in the $M^{+\cdot}$ cluster must be within 20% of the theoretical. [If target compound amounts are low and the MS is operated at high sensitivity, the cluster pattern may deviate from theory. The utility of this criterion is also diminished in the case of BCDD/Fs, where the patterns often resemble those of the more highly chlorinated analogues (Tong, 1991b)].

(v) Absence of interferences from PBDPEs during PBDF analysis, or from xanthenes during PBDD analysis, should be demonstrated by monitoring an intense peak of the PBDPE $M^{+\cdot}$ cluster, or of the xanthene $[M-H]^{+\cdot}$ cluster, respectively.

For the analysis of PBDD/Fs in flame retardant chemicals, the EPA test rule requires recoveries of analytes to be in the range 50% to 150% and a signal-to-noise ratio of $\geq$ 3 for all monitored m/z. Other quality assurance requirements have been summarized (Tondeur, 1990).

4.0 ENVIRONMENTAL DISTRIBUTION AND FATE

The fact that BCDD/Fs have been found in waste incinerator fly ash samples and in motor vehicle exhaust emissions suggests that such species may be as widely dispersed in the environment as the PCDD/Fs, but at lower levels. The shift from leaded to unleaded gasoline should result in a reduction of the levels of the brominated congeners.

The PBDD/Fs may tend to have a more localized distribution since they are most likely to be produced as a result of accidental fires involving flame-retardant-treated materials. As with the PCDD/Fs, atmospheric transport is likely to be a major mode of dispersal of the PBDD/Fs and BCDD/Fs in the environment. In connection with studies aimed at modelling the environmental fate and incineration behaviour of halogenated DD/Fs, vapour pressure measurements have been performed on some congeners and the resulting data used in a correlation method for predicting the vapour pressures of other congeners (Rordorf, 1987, 1989, 1990). Calculated, or estimated, values of octanol/water partition coefficients indicate that while bromine-containing DD/Fs are somewhat more lipophilic than the chloro analogues, there should be no large differences in ecological behaviour among chlorinated, brominated and mixed halogenated DD/Fs (Fiedler, 1990).

Since C-Br bonds are less stable than C-Cl bonds, PBDD/Fs and BCDD/Fs should be more susceptible to destruction by sunlight-induced photolysis than the PCDD/Fs. Such a process may represent a significant degradation pathway for the brominated congeners in the environment. Indeed, both PBDD/Fs and BCDD/Fs have been found to undergo rapid

reaction upon irradiation in dilute hydrocarbon solution with either full sunlight (Buser, 1988) or low pressure mercury lamps (Lenoir, 1991). In the major products of these reactions, bromine had been replaced by hydrogen so that, for example, photolysis of BCDD/Fs would give PCDD/Fs. The rate of hydrodebromination generally decreased (moderately) with decreasing bromine content of the starting molecule (Lenoir, 1991) and the results were used to derive an estimate of the photochemical fate of PBDD/Fs on lipophilic environmental surfaces (e.g. plant waxes). Photolysis in methanol (considered to be a model for aqueous systems) proceeded nearly six times more slowly than in n-hexane (Lenoir, 1991). Photolysis of PBDD/Fs and BCDD/Fs deposited on quartz surfaces (Buser, 1988), or of PBDD/Fs adsorbed on soot particles (Lutes, 1992a, 1992b) upon exposure to sunlight proceeded much more slowly (if at all in the latter case).

Other than two cases of localized exposure (Schecter, 1991; refs 26 and 27 in Wiberg, 1992), there appears to be no reports of the detection of PBDD/Fs or BCDD/Fs in living organisms. In a recent investigation of muscle samples from salmon and osprey, and of human mothers' milk (Wiberg, 1992), no brominated congeners could be detected (limits of detection < 1 ppt in most cases), while PCDD/Fs were found in all samples analyzed. In a study of human adipose tissue samples (Cramer, 1990; Stanley, 1991), PBDD/Fs could not be detected, but PBDPEs (ppt to low ppb levels) were found. The failure to detect PBDD/Fs or BCDD/Fs may reflect, inter alia, lower emission levels compared to PCDD/Fs, differences in photochemical decomposition rates, and differences in uptake, metabolism and excretion. Waste incinerators, the main source of PCDD/Fs, have been estimated to

produce ca. 1-20% as much of the bromine-containing analogues (Donnelly, 1990a).

In connection with the possibility of loss by photochemical decomposition, it is worth noting that other polybrominated aromatic derivatives have been found in biota; PBDPEs were found in fish caught in Swedish waters (Andersson, 1981) and in the North Sea (de Boer, 1989) and both PBDPEs and polybrominated biphenyls were detected in seals, guillemots and white-tailed sea eagles from the Baltic, North Sea and Arctic Ocean (Jansson, 1987). Brominated aromatics have also been found in more localized sites; eg. pentabromotoluene in sewage sludge (Mattson, 1975), tetrabromobisphenol A in river and nearby marine sediments (Watanabe, 1983) and $Br_{10}DPE$ in river sediment (Watanabe, 1986). These results indicate the polybrominated aromatic derivatives are widely distributed in the environment and can have sufficiently long lifetimes in the environment to allow entry into the food chain.

5.0 BIOLOGICAL AND TOXICOLOGICAL EFFECTS

Clearly, recognition of the potentially severe health hazards associated with the PCDD/Fs has stimulated interest in the PBDD/Fs and BCDD/Fs. Thus, much of the research effort devoted to the investigation of the biological and toxicological properties of the brominated congeners has focussed on the qualitative and quantitative comparison of their activities with those of the PCDD/Fs. The results obtained to date indicate that the characteristic features of PCDD/F toxicity (eg. species differences, delayed onset, chloracne, hepatic porphyria, edema in young chickens, thymic involution, teratogenicity) are also found with the PBDD/Fs and BCDD/Fs. However, since there are few toxic responses which are dose-related, quantitative, and easily measured, most investigations of the potencies of these compounds have involved the measurement of biochemical responses such as induction of the enzymes d-aminolevulinic acid synthetase (ALA synthetase), aryl hydrocarbon hydroxylase (AHH) or ethoxyresonifin-O-deethylase (EROD). There is, in general, good correspondence between the potency of enzyme induction elicited by a toxic compound and its toxic potency, although kinetic factors may complicate the picture (Neubert, 1991). Reports of biological/toxicological studies involving PBDD/Fs, BCDD/Fs and PCDD/Fs are summarised in Table 6.

In the earliest report from the surveyed literature (1973) concerning the biochemical effects of PBDD/Fs (Poland, 1973a), 2,3,7-Br_3DD and several PCDDs were compared for their ability to induce ALA synthetase and AHH in the livers of chick embryos. Compounds which induce the former enzyme also cause hepatic porphyria (a common ailment among

TABLE 6*

Biological and Toxicological Studies of PBDD/Fs and BCDD/Fs

Reference	Compounds Investigated	Media or Organisms Involved	Observations
Blankenburg, 1990	2,3,7,8-tetra(bromo/chloro) DDs	Primary cell cultures of rat hepatocytes	None of the tested ocngeners was more active than 2,3,7,8-Cl_4DD in the induction of EROD activity.
Denomme, 1985	7-X-2,3-Cl_2DDs (X = Br, Cl, F, H, I, OH, OMe, NH_2, NO_2, Cn, CO_2Me, CH_3, t-Bu, Ph, CF_3, or 7,8-$(CH)_4$)	Rat hepatoma H-4-II E cells in culture. Hepatic cytosol.	No rank order correlation between TCDD receptor binding EC_{50} values and induction of AHH or EROD activities. Data could be correlated with an estimate of substituent (X) width.
Denomme, 1986	8-X-2,3-Cl_2DFs (X = Br, Cl, F, H, I, CH_3, i-Pr, t-Bu, OH, OMe) and 8-X-2,3,4-Cl_3DFs (X = as above, and C_2H_5, CH_2Br, CF_3)	Rat hepatoma H-4-II E cells in culture. Hepatic cytosol.	TCDD receptor binding affinities dependent only upon substituent (x) lipophilicities. AHH and EROD induction activities both substituent- and chlorine substitution pattern-dependent.
Ivens, 1990	2,3,7,8-Br_4DD	Male Wistar rats (subchronic toxicity study with daily doses of 0.01, 0.1, 1, 3 and 10 μg/kg body wt for up to 91 days)	Poor survival rate at 10 μg/kg dose rate. Wasting syndrome, slight anemia, reduced blood clotting time, thymus atrophy, depletion of lymphocytes in thymus and spleen, peliosis hepatis at 3 or 10 μg/kg. Rapid elimination of Br_4DD from livers of animals allowed to recover - half-life in liver apparently lower than that of TCDD.
Kende, 1973, 1974	2,3,7-Br_3DD; 2,3,7,8-Br_4DD; 2,3,-Br_2-7,8-Cl_2DD; PCDDs; other substituted DDs	Chicken embryos (liver)	SARs of bromo congeners for AHH induction: 0.6:1.0:1.1 (TCDD = 1.0)

*TCDD is used here to denote 2,3,7,8-Cl_4DD

TABLE 6 (cont.)

Loser, 1989	2,3,7,8-Br_4DD	Male and female Wistar rats (subchronic toxicity study; doses of 0.01, 0.1, 1, 3 or 10 μg/kg body wt administered by gavage for up to 90 consecutive days)	Mortality at the 3 and 10 μg dose rates - LD_{50} appears to lie between these values. Toxicity 3- to 10-fold lower than that of TCDD. Reduced weight gain or relative thymus weight only at doses >0.1 μg/kg. Serum thyroxine and triiodothyronine levels decreased and increased, respectively, at doses >0.01 μg/kg.
Mason, 1987a	2-BrDD; 2,7/2,8-Br_2DD; 2,3,7-Br_3DD; 1,3,7,8-Br_4DD; 1,3,7,9/2,4,6,8-Br_4DD; 2,3,7,8-Br_4DD; 1,2,3,7,8-Br_5DD; 1,2,4,7,8-Br_5DD; 2,3-Br_2-7,8-Cl_2DD; 2,8-Br_2-3,7-Cl_2DD; 2-Br-3,7,8-Cl_3DD	Hepatic cytosol (TCDD receptor binding affinities). Immature male Wistar rats (AHH and EROD induction; body wt loss; thymic atrophy).	Binding affinities not significantly altered by interchange of Br and Cl. 2,3,7,8-Br_4DD was the most toxic compound of the series with a potency comparable to that of TCDD.
Mason, 1987b	As in Mason, 1987a	Rat hepatoma H-4-II E cells (TCDD receptor binding; AHH and EROD induction). Immature male Wistar rats (thymic atrophy; body wt loss; hepatic microsomal AHH and EROD induction).	For PBDDs or BCDDs, SARs were comparable both for in vivo responses and for in vitro binding and AHH induction. Linear correlation between -logEC_{50} (in vitro AHH induction) vs in vivo -logED_{50} (thymic atrophy) and -logED_{50} (body wt loss).
Moore, 1979	2,3,7,8-Br_4DF; 2,3,7,8-Cl_4DF; 2,3,4,7,8-Cl_5DF	Guinea pigs (single oral dose in corn oil).	Pattern of toxic symptoms similar for all three compounds at comparable dose levels.
Nagao, 1990a	2,3,7,8-Br_4DD; 2,3,7,8-Cl_4DD	Female Wistar rats (single subcutaneous injection; EROD induction).	Time dependence of the induction profile of EROD activity almost identical after injection of 600 ng Br_4DD or 300 ng TCDD/kg body wt. Extent of EROD induction linear for 0.02 to 6 nmol Br_4DD/kg body wt.

TABLE 6 (cont.)

Nagao, 1990b	2,3,7,8-Br_4DD	Rats (single subcutaneous injection of <1 μg/kg body wt)	Induction of hepatic monooxygenases.
Nagao, 1990c	2,3,7,8-Br_4DD; 2,3,7,8-Cl_4DD	Mice.	Similar potencies in induction of cleft palate. With single doses, no higher potency was found for the brominated congener on a molar basis, but kinetics appear to be different (brominated congener more persistent in adipose tissue).
Poland, 1973a, 1973b	2,3,7-Br_3DD; PCDDs	Chick embryos (induction of ALA synthetase and AHH activities in liver).	Bromo derivative shows activity comparable with that of TCDD and significantly greater than that of 2,3,7-Cl_3DD. Perfect correspondence between whole animal toxicity data and enzyme induction potencies.
Romkes, 1987a	2-X-3,7,8-Cl_3DD (X = Br, Cl, F, H, I, OH, OMe, NH_2, NHAc, NO_2, CH_3, CN, CF_3)	Hepatic cytosol from rat, mouse, guinea pig and hamster (TCDD receptor binding affinities). Rat hepatoma H-4-II E cells in culture (receptor binding; AHH induction).	Important species differences in receptor protein binding site interactions with the variously substituted derivatives. Correlation between acceptor binding and AHH induction dependent on a steric parameter for the 2-substituent.
Romkes, 1987b	As in Romkes, 1987a	Rat hepatic cytosol (TCDD receptor binding). Immature male Wistar rats (AHH induction, thymic atrophy; body wt loss).	Receptor binding pEC_{50}, X = Br (6.94), Cl (8.00), CF_3 (8.50; highest value found). The 2-halo substituted derivatives were all highly toxic, but the most active compound was 2-F_3C-3,7,8-Cl_3DD.
Safe, 1989	2,3,7,8-Br_4DD; 2,3-Br_2-7,8-Cl_2DD; 2-Br-3,7,8-Cl_3DD; 1,2,3,7,8-Br_5DD; 1,2,4,7,8-Br_5DD; 1,3,7,8-Br_4DD; extracts of pyrolysates from brominated flame retardants, and of fly ash from a municipal waste incinerator.	Rat hepatoma H-4-II E cells in culture (AHH and EROD induction). Immature male Wistar rats (AHH induction; body wt, thymic atrophy), guinea pigs (AHH induction; body wt), and mice (immunotoxicity).	Correlation of in vitro induction potencies with in vivo biologic and toxic effects. Development of assay system to quantitate TCDD equivalents present in extracts from various sources.

TABLE 6 (cont.)

Schecter, 1991	2,3,7,8-Br_4DD; 2,3,7,8-Cl_4DD	Human subject exposed to these compounds (34 years after initial exposure)	Serum lipid levels of 1100 ppt bromo and 20 ppt chloro derivative. Estimated initial exposure levels in ranges 11,606 - 122,450 ppt and 158 - 1670 ppt respectively, assuming 5-10 year half-life. Symptoms at the time of exposure - chloracne, headaches, back and leg pain upon exertion, nausea. Blood chemistry appeared normal and subject made a rapid recovery.
Schulz-Schalge, 1991	2,3,7,8-Br_4DD; 2,3,7-Br_3-8-ClCDD; 2,3-Br_2-7,8-Cl_2DD; 2-Br-3,7,8-Cl_3DD; 2,3,7,8-Cl_4DD	Male Wistar rats (EROD induction in liver following a single subcutaneous administration).	All five compounds show similar potencies for EROD induction. Use of a substrate concentration of 0.5 μM ethoxyresorufin in assays is recommended - substrate inhibition observed at commonly used 5 μM. Maximum for EROD induction was observed 7 days after administration of dioxins (Naunyn Schmiedebergs Arch. Pharmacol., in press, 1991).
Zacharewski, 1988	Pyrolysates from fire-retardants. FR 300 BA (Br_{10}DPE); Firemaster BP-6 (polybrominated biphenyls); Bromkal 70-DE (mainly Br_4/Br_5DPE); Bromkal 70-5 DE (mainly Br_5DPE); Bromkal G1 (Br_5DPE)	Rat hepatoma H-4-II E cells in culture (AHH and EROD induction). Immature male Wistar rats (hepatic microsomal AHH and EROD induction; body wt loss; thymic atrophy).	Protocol for the determination of "TCDD equivalents" by comparing relative induction activities of pyrolysates with that of TCDD. In vivo dose-response effects determined for pyrolysates from Firemaster BP-6 and Bromkal 70-5 DE.

workers in a factory producing 2,4,5-T due to concommitant generation of 2,3,7,8-Cl_4DD), as well as inducing microsomal mixed-functional oxygenase activity in the liver. The latter type of activity is associated with the so-called "drug metabolizing enzymes", which include AHH. The results of this investigation led to the following conclusions:

(i) All compounds that are, on the basis of other studies, lethal, teratogenic or acneogenic, induce ALA synthetase.

(ii) The relative potencies for ALA synthetase induction closely parallel those for AHH induction,

(iii) Congeners with halogen atoms in at least 3 of the four lateral positions (ie. 2,3,7,8) and having at least one free non-halogenated carbon, are active as inducers.

Of particular interest in this report is the finding that 2,3,7-Br_3DD is almost as potent an inducer as the most active congener tested, 2,3,7,8-Cl_4DD (TCDD), and significantly more potent than the trichloro analogue 2,3,7-Cl_3DD.

In an extension of the initial study (Poland, 1973b), it was concluded that there is "a perfect correspondence between the whole animal toxicity data on the dioxin congeners and their ability to induce both enzymes". The results of these and further studies on a wider range of substituted derivatives (Kende, 1973, 1974) suggest that, for different substituents in the lateral positions of the dioxin molecule, the order of relative potencies in Br>Cl>F>NO_2. It was further proposed that combination of a dioxin derivative with an "induction receptor" is required to initiate the event, or events, leading to the observed increase in enzyme activity. Subsequently, as a result of work on the PCDD/Fs, particularly the highly toxic

2378-TCDD, it was proposed (Poland, 1979, 1982) that the mode of action of the dioxins, and structurally related compounds, involves initial binding or complexation with a cytosolic receptor protein (the TCDD receptor), followed by translocation of the complex to the cell nucleus. Once in the nucleus, the complex can interact with the cellular DNA, and influence the expression of activities of a battery of enzymes. Accumulated evidence indicates that the receptor site on the DNA (Ah receptor) is involved in the induction of AHH and also plays a role in mediating many of the toxic effects elicited by TCDD. Cytosolic TCDD-receptor protein has been identified in various tissues from a range of animal species and from human and mammalian cells in culture.

In a paper published in 1979 (Moore, 1979), the toxic effects of single oral doses of 2,3,7,8-Br_4DF, 2,3,7,8-Cl_4DF and 2,3,4,7,8-Cl_5DF in guinea pigs were compared. All three compounds were lethal at low doses (15.84 μg/kg body wt. for the tetrabromo congener and 10 μg/kg for the tetrachloro congener), and the toxic symptoms produced were noted to be similar for all three components at comparable dose levels.

Further reports on the biological and toxicological effects of PBDD/Fs and BCDD/Fs began to appear only in 1985. Using receptor binding, enzyme induction, and other assays (both in vitro and in vivo), Safe and coworkers have obtained quantitative data on the relationship between structure and activity for a wide range of dioxin and dibenzofuran derivatives prepared in their laboratories. Much of this information was obtained using hepatic cytosol, rat hepatoma cells in culture and immature male Wistar rats.

In the first of these studies (Denomme, 1985), sixteen 7-substituted-2,3-Cl_2DDs were tested for their TCDD-receptor binding affinities and AHH and EROD induction potencies. The 7-bromo congener was found to be the most active inducer and an excellent linear correlation was found between the AHH and EROD induction potencies for this group of compounds. While there was not a rank order correlation between AHH induction potency and receptor binding affinity, a quantitative structure activity relationship (QSAR) was developed by including a substituent width parameter in the equation. Similar studies on a series of 8-substituted-2,3-Cl_2DFs and 8-substituted-2,3,4-Cl_3DFs indicated that bromo- and chloro-substituted compounds had very similar binding affinities and induction potencies (Denomme, 1986). Again, the QSARs developed for the latter were dependent upon a substituent width parameter. Receptor binding affinities and AHH induction activities were also determined for a series of thirteen 2-substituted-3,7,8-Cl_3DDs (Romkes, 1987a, 1987b). Interestingly, while the 2-halo (F, Cl, Br, I) derivatives in this series were all highly toxic, the most active derivative was 2-F_3C-3,7,8-Cl_3DD, which also had the highest TCDD-receptor binding affinity. Comparison of binding affinities for receptors from different species (rat, mouse, quinea pig, hamster) indicated that there are important structural differences in the hepatic cytosolic receptor protein ligand binding sites in these species. Related studies, devoted exclusively to PBDDs and BCDDs (Mason, 1987a, 1987b), and including a comparison of in vitro and in vivo activities in rats, led to the following conclusions:

(i) The congeners with bromine or chlorine in all four lateral positions tended to have the highest binding affinities, exceptions being 2,3,7-Br_3DD and 2-Br-3,7,8-Cl_3DD which showed relatively high and low affinities, respectively.

(ii) The structural factors that govern the toxicities of the PCDDs (eg. lateral positions substituted, decrease in potency with non-lateral substitution) also apply to the PBDDs and BCDDs.

(iii) While similarly substituted PBDDs and BCDDs tend to have similar potencies to the analogous PCDDs, in some cases the brominated congeners are more active.

(iv) As found earlier for PCDD/Fs, plots of $-\log EC_{50}$ (in vitro AHH induction) vs $-\log EC_{50}$ (in vivo AHH induction), $-\log ED_{50}$ (thymic atrophy), or $-\log ED_{50}$ (body wt. loss) were linear.

(v) The results in (iv) indicate that the in vitro AHH induction bioassay may be used to estimate the potential in vivo toxicities of PBDDs, BCDDs, or other halogenated aromatic derivatives relative to TCDD, that is, to determine "TCDD equivalents".

Much of this work, and related work on other halogenated aromatic derivatives, has been summarized in a review (Safe, 1989). In this review, the development of the in vitro AHH induction assay for quantitating TCDD equivalents for individual toxic halogenated aromatic derivatives, and its application to complex mixtures such as those obtained by extraction of waste incinerator fly ash, or upon pyrolysis of brominated flame retardants (Zacharewski, 1988) are discussed.

More recently, in work related to that described above, several authors (Blankenburg, 1990; Nagao, 1990a, 1990b; Schulz-Schalge, 1991) have investigated the relative potencies of 2,3,7,8-Br_4DD, TCDD, and analogously-substituted mixed bromochloro derivatives in the induction of EROD, both in vitro (primary cultures of rat hepatocytes) and in vivo (male and female Wistar rats). Those studies indicate that, for all congeners, a maximum in EROD induction occurs ca. 7 days after a single administration of halogenated dioxin, and

that all congeners tested have similar activities. At most dose levels, none of the congeners tested had greater activity than TCDD. In one report (Schulz-Schalge, 1991), it was noted that the kinetics of the EROD reaction in microsomes from non-induced rat livers was different from that of the induced animals, indicating the existence of at least two different enzymes catalyzing the conversion of ethoxyresorufin to resorufin in liver microsomes of male rats. Further studies indicated that EROD in microsomes of TCDD-induced rats exhibited a pronounced substrate inhibition at ethoxyresorufin concentrations exceeding 2μM. It was therefore strongly recommended that EROD induction studies be carried out at a substrate concentration of 0.5 μM instead of 5 μM as commonly employed for routine studies.

The results of a three-month subchronic toxicity study of 2,3,7,8-Br_4DD in both male and female Wistar rats (Ivens, 1990; Loser, 1989), including comparison with the effects of TCDD, indicate that the bromodioxin is 3- to 10-fold less toxic with an LD_{50} estimated to be ca 3-10 μg/kg body weight. (An acute toxicity study of 2,3,7,8-Br_4DD gave an LD_{50} of ca. 300 μg/kg for male rats and 100 μg/kg for female rats). The toxic symptoms produced by the bromodioxin (see Table 6) are typical of those normally associated with TCDD. However, it was found that the bromodioxin was eliminated more rapidly than TCDD from the livers of animals allowed to recover from treatment. A concommitant study of the storage of 2,3,7,8-Br_4DD in liver and adipose tissues indicated that the dioxin is accumulated time dependently and in proportion to dose level. An investigation of the relative potencies of 2,3,7,8-Br_4DD and TCDD for the induction of cleft palate in mice indicates that the two

congeners are similar (Naga, 1990c). However, it was observed that, with single doses, no higher potency was found for the bromodioxin on a molar basis. As noted in the above studies on rats, the kinetics appear to be different for the bromo and chloro derivatives.

There would appear to be only two reports on the biochemistry or toxicology of bromine-containing dioxins or dibenzofurans in human subjects. In the earlier of these (Schecter, 1991), elevated levels of 2,3,7,8-Br_4DD, and, to a lesser extent, of TCDD, were measured in the blood of a chemist who had synthesized relatively large quantities of both compounds 34 years previously. At the time, he was hospitalized with sever symptoms of dioxin poisoning (see Table 6), but apparently made a rapid recovery and was, at the time of the report, in good health. Estimates of the body burden present at the time of hospitalization, and the lack of fatal outcome, suggest that human beings are not among the more "dioxin-sensitive" mammals such as the guinea pig. In the later report (Zober, 1991a, 1991b; through Wiberg, 1992, refs 26 and 27), PBDD/Fs were found in the blood of employees exposed to these compounds during extrusion blending of resins containing Br_{10}DPE. The two examples indicate that occupational exposure probably represents the greatest threat to human health from bromine-containing dioxins or dibenzofurans.

6.0 SUMMARY/CONCLUSIONS

Until proven otherwise, it would be safe to assume that the PBDDs, PBDFs, BCDDs and BCDFs, in large part, mimic the PCDDs and PCDFs.

Toxicologically, they should be considered to be equipotent. The biological effects of the compounds studied to date are very similar to those elicited by their chloro analogues. And, although only limited data is available, it would seem that these compounds are retained in exposed mammals.

It has been proven that the major sources of these compounds parallel those of the PCDDs and PCDFs. They are not made intentionally, but are found as impurities in commercial chemicals and are combustion byproducts when certain precursors are present.

The PBDD/Fs and BCDD/Fs are likely entering the environment (they have been found in fly ash and in exhaust from internal combustion engines). However, there is no evidence, as yet, that they have entered the food chain.

The levels of these compounds in the environment are expected to be much lower than those of the PCDDs and PCDFs. For example, they have been found in fly ash, but at levels that are much less than 10% of the PCDD/PCDF levels. Moreover, these compounds probably would degrade faster in the environment and are susceptible to chlorine-for-bromine exchange.

The analytical methods currently used for PCDDs and PCDFs, with some modifications, can be used for the analysis of PBDDs, PBDFs, BCDDs and BCDFs. Presently, there are only a small number of commercially available analytical standards (and surrogates) which severely hampers the development of newer and more rigorous methods. It is doubtful that many additional standards will be made available commercially, unless the interest in these compounds increases.

7.0 RECOMMENDATIONS FOR FUTURE RESEARCH

It is the opinion of the authors of this report that some limited studies are needed to determine if, and to what extent, the PBDDs, PBDFs, BCDDs and BCDFs pose a threat to human health and the environment in Ontario and Canada.

In order of priority, the following research projects are recommended:

(1) The amounts of brominated flame retardants, and other organo-bromine compounds, that are manufactured, imported and used in Ontario (and Canada) should be determined. If they are used to a significant extent, the chemical precursors for the PBDD/Fs and BCDD/Fs would be present.

(2) If from (1) it is determined that brominated flame retardants are being used, occupational surveys (and monitoring if considered necessary and feasible) should be initiated. The literature indicates that the processes whereby brominated flame retardants are incorporated into certain materials (eg. plastics) may be a source of PBDDs and PBDFs.

(3) Selected samples, of an Ontario origin, should be screened for PBDDs, PBDFs, BCDDs and BCDFs using HRGC/HRMS methods. These should include samples of brominated flame retardants (in use in Ontario or Canada; see (1)) and fly ash from waste incinerators.

It is also recommended that incinerator feed stocks be analyzed for total bromine, total organic bromine and selected brominated flame retardants.

It is probable, particularly relative to PCDDs and PCDFs, that the PBDDs, PBDFs, BCDDs and BCDFs are not a significant environmental and health hazard. The studies listed above would serve to prove (or disprove) this theory.

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